

CLAIMS

1. Isolated antibodies and antisense oligonucleotides that recognize or modulate BAG3 protein and fragments thereof characterized in that they are used in research, diagnostics and therapy for cell death-involving diseases, and for modulation of cell survival and/or death, said protein and fragments being selected in the group of peptide sequences identified as SEQ ID NO: 2, 4, 6, 8, 15, 16, 17, 18.
2. Antibodies and antisense oligonucleotides according to claim 1 wherein said protein and fragments have a homology of at least 75%, preferably at least 80% homology, preferably at least 90% homology, more preferably at least 95% homology, even more preferably at least 98% homology to at least one of the BAG3 protein and fragments selected in the group of sequences identified as SEQ ID NO: 2, 4, 6, 8, 15, 16, 17, 18.
3. Antibodies and antisense oligonucleotides according to claims 1-2 for modulating apoptosis in primary cells.
4. Antibodies and antisense oligonucleotides according to claims 1-3 for use in the treatment of a disease selected in the group of: acute or chronic tissue damages, such as heart, kidney, brain or other organ ischaemia, HIV- related damage of brain or other tissues, skeletal muscle disorders, transplantation rejection; chronic degenerative disorders such as Parkinson's disease, amyotrophic lateral sclerosis and others; and neoplastic, autoimmune and other diseases involving excessive or defective apoptosis; tissue repair or wound healing, treatment of surgical incisions, and ulcers, such as stomach or diabetic ulcers.
5. Isolated polynucleotides encoding the protein and fragments according to claims 1-4.
6. Antibody according to claims 1-4 selected in the group of polyclonal antibodies AC-BAG3-1 and AC-BAG3-2 and monoclonal antibodies from mother clones AC-1, AC-2, AC-3, AC-4, AC-5, AC-6, AC-7, AC-8, AC-9 against at least one of the peptide sequences indicated as SEQ ID NO: 2, 4, 6, 8, 15, 16, 17, 18.
7. Antibody AC-1- derived according to claim 6 secreted by the hybridoma **mother clone** n° PD02009 deposited on the 17/12/2002 at the Centro

Biotechnologie Avanzate di Genova.

8. Hybridoma mother clone n° PD02009 deposited on the 17/12/2002 at the Centro Biotechnologie Avanzate di Genova for the production of the antibody according to claim 7.
- 5 9. Map construct to obtain the antibodies according to claims 6-7, said construct being selected in the group of:
 - MAP-BAG3-1: nh2-DRDPLPPGWEIKIDPQ-MAP containing (SEQ ID NO 15)
 - MAP-BAG3-2: nh2- SSPKSVATEERAAPS-MAP containing (SEQ ID NO 16)
 - MAP-BAG3-3: nh2- DKGKKNAGNAEDPHT-MAP containing (SEQ ID NO 17)
 - 10 - MAP-BAG3-4: nh2- NPSSMTDTPGNPAAP-MAP containing (SEQ ID NO 18)
10. Antisense oligonucleotides according to claims 1-4 having a sequence selected in the group of SEQ ID NO: 9, 10, 11.
11. A vector comprising the isolated oligonucleotide/s of claim 10.
12. An expression vector comprising the isolated oligonucleotide/s of claim 10.
- 15 13. A host cell genetically engineered to contain the oligonucleotide/s of claims 1-8.
14. A host cell genetically engineered to contain the oligonucleotide/s of claim 10 in operative association with a regulatory sequence that controls expression of the oligonucleotide in the host cell.
- 20 15. Polynucleotides and corresponding codified peptides indicated as SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 15, 16, 17, 18 and constructs comprising them to modulate cell survival and/or death in primary cells.
16. Composition for use as a medicament for modulating the BAG3 expression characterized in that it comprises as active principle at least one antibody or
- 25 antisense oligonucleotide according to claims 1-7 or polynucleotides and polypeptides according to claim 15.
17. Composition according to claim 16 characterized in that it comprises the monoclonal antibody AC-1.
18. Composition according to claims 16 and 17 characterized in that it contains an
- 30 antibody against a peptide sequence selected in the group of SEQ ID NO: 2, 4, 6, 8, 15, 16, 17, 18.
19. Composition according to claims 16-18 further comprising a pharmaceutically acceptable carrier.

20. Composition according to claims 16-19 for cell death-involving diseases, and for modulation of cell survival and/or death
21. Composition according to claims 16-20 for modulating apoptosis in primary cells.
- 5 22. Composition according to claims 16-21 for use in the treatment of a disease selected in the group of: acute or chronic tissue damages, such as heart, kidney, brain or other organ ischaemia, HIV- related damage of brain or other tissues, skeletal muscle disorders, transplantation rejection; chronic degenerative disorders such as Parkinson's disease, amyotrophic lateral
- 10 sclerosis and others; and neoplastic, autoimmune and other diseases involving excessive or defective apoptosis; tissue repair or wound healing, treatment of surgical incisions, and ulcers, such as stomach or diabetic ulcers.
23. A diagnostic agent to determine the expression of BAG3 protein characterized in that it contains a monoclonal or polyclonal antibody directed against the
- 15 polypeptide sequence selected in the group of SEQ ID NO: 4, 6, 8, 15, 16, 17, 18, preferably as defined by AC-1.
24. Use of antibodies and antisense oligonucleotides according to claims 1-7 or or polynucleotides and polypeptides according to claim 15 in research, diagnostics and therapy for cell death-involving diseases, and for modulation of
- 20 cell survival and/or death.
25. Use of antibodies and antisense oligonucleotides according to claims 1-7 or or polynucleotides and polypeptides according to claim 15 for modulating apoptosis in primary cells.
26. Use according to claims 24-25 to treat a disease selected in the group of: acute
- 25 or chronic tissue damages, such as heart, kidney, brain or other organ ischaemia, HIV- related damage of brain or other tissues, skeletal muscle disorders, transplantation rejection; chronic degenerative disorders such as Parkinson's disease, amyotrophic lateral sclerosis and others; and neoplastic, autoimmune and other diseases involving excessive or defective apoptosis;
- 30 tissue repair or wound healing, treatment of surgical incisions, and ulcers, such as stomach or diabetic ulcers.
27. Method for detecting the presence of the nucleotide sequence SEQ ID NO: 1 or of the protein SEQ ID NO: 2 or parts of them in a sample, in particular at

least a part identified as SEQ ID NO: 3, 4, 5, 6, 7, 8, 15, 16, 17, 18; said method comprising the steps of: contacting the sample with a compound that binds to and forms a complex with the nucleotide or the protein or parts thereof in sufficient conditions to form the complex, and detecting said complex.

- 5 28. Method for detecting a compound that binds to the protein SEQ ID NO: 2 or parts of it in a sample, in particular at least a part identified as SEQ ID NO: 4, 6, 8, 15, 16, 17, 18; said method comprising the steps of: contacting the compound with the protein or its part/s in sufficient conditions to form the complex compound/protein or its part/s, and detecting said complex.
- 10 29. Kit for identification and diagnosis comprising the polyclonal or monoclonal antibodies according to claims 1-7 or nucleotide sequence SEQ ID NO: 1 or the protein SEQ ID NO: 2 or parts of them, in particular at least a part identified as SEQ ID NO: 3, 4, 5, 6, 7, 8, 15, 16, 17, 18; or the antisense and nonsense oligos identified as SEQ ID NO: 9, 10, 11, 12, 13, 14, or functionally
- 15 equivalents of the above identified sequences.